40. (Amended) A gene-targeted, non-human rodent homozygous for a human Familial Alzheimer's Disease (FAD) mutation comprising a human mutation of the presenilin-1 (PS-1 gene), and a human transgenic for Swedish APP695, wherein the Aβ42 protein level is elevated relative to the Aβ42 protein level in a wild-type rodent.

41. (Amended) The rodent of claim 39 wherein said mutation of said PS-1 gene is P264L.

42. (Amended) The rodent of claim 40 wherein said mutation of said PS-1 gene is P264L

44. (Amended) The rodent of claim 43 wherein said rodent is a mouse.

46. (Amended) The rodent of claim 45 wherein said rodent is a mouse.

47. (Amended) Generational offspring of the rodent of claim 39 wherein said mutant PS-1 gene is expressed.

48. (Amended) Generational offspring of the rodent of claim 40 wherein said mutant PS-1 gene is expressed.

49. (Amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of the Aβ peptide, said method comprising the steps of:

a) administering said chemical compound to the rodent of claim 39; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

50. (Amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of the Aβ peptide, said method comprising the steps of:

a) administering said chemical compound to the rodent of claim 40; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

51. (Amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of the Aβ peptide, said method comprising the steps of:

Q3

a) administering said chemical compound to the rodent of claim 47; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

52. (Amended) A method for screening chemical compounds for the ability to decrease *in vivo* levels of the Aβ peptide, said method comprising the steps of:

a) administering said chemical compound to the rodent of claim 48; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

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57. (Amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the rodent of claim 39; and

Q4

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

58. (Amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the rodent of claim 40; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

59. (Amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the rodent of claim 47; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

Q4 wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

60. (Amended) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:

a) administering a compound to the rodent of claim 48; and

b) measuring the amount of Aβ peptide in a tissue sample from said rodent,

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

77. (New claim) A gene-targeted rodent heterozygous for a human presenilin-1 (PS-1) mutation and comprising a human Swedish mutation, said rodent comprising in its genome:

a DNA sequence encoding a PS-1 protein comprising the human P264L mutation; and

Q5 a DNA sequence encoding a human amyloid precursor protein having the Swedish APP695 mutation;

wherein the Aβ42 protein level is elevated relative to the Aβ42 protein level in a wild-type rodent.

78. (New claim) The rodent of claim 77 wherein said rodent is a mouse.

79. (New claim) The rodent of claim 77 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

80. (New claim) The rodent of claim 79 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

81. (New claim) The rodent of claim 77 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

82. (New claim) A generational offspring of the mouse of claim 77 wherein said offspring comprises in its genome:

a DNA sequence encoding a PS-1 protein comprising the human P264L mutation; and

a DNA sequence encoding a human amyloid precursor protein having the Swedish APP695 mutation;

wherein the Aβ42 protein level is elevated relative to the Aβ42 protein level in a wild-type rodent.

83. (New claim) A gene-targeted rodent homozygous for a human presenilin-1 (PS-1) mutation and comprising a human Swedish mutation, said rodent comprising in its genome:

a DNA sequence encoding a PS-1 protein comprising the human P264L mutation; and

a DNA sequence encoding a human amyloid precursor protein having the Swedish APP695 mutation;

wherein the Aβ42 protein level is elevated relative to the Aβ42 protein level in a wild-type rodent.

84. (New claim) The rodent of claim 83 wherein said rodent is a mouse.

85. (New claim) The rodent of claim 83 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

86. (New claim) The rodent of claim 85 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.

87. (New claim) The rodent of claim 83 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

88. (New claim) A generational offspring of the mouse of claim 83 wherein said offspring comprises in its genome:

a DNA sequence encoding a PS-1 protein comprising the human P264L mutation; and

a DNA sequence encoding a human amyloid precursor protein having the Swedish APP695 mutation;

wherein the Aβ42 protein level is elevated relative to the Aβ42 protein level in a wild-type rodent.

89. (New claim) A method for screening a compound for the ability to decrease *in vivo* levels of the Aβ peptide comprising the steps of:

administering said compound to the rodent of claim 77; and

measuring the amount of Aβ peptide in a tissue sample from said rodent;

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

90. (New claim) A method for screening a compound for the ability to decrease *in vivo* levels of the Aβ peptide comprising the steps of:

administering said compound to the rodent of claim 82; and

measuring the amount of Aβ peptide in a tissue sample from said rodent;

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

91. (New claim) A method for screening a compound for the ability to decrease *in vivo* levels of the Aβ peptide comprising the steps of:

administering said compound to the rodent of claim 83; and

measuring the amount of Aβ peptide in a tissue sample from said rodent;

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

92. (New claim) A method for screening a compound for the ability to decrease *in vivo* levels of the Aβ peptide comprising the steps of:

administering said compound to the rodent of claim 88; and

measuring the amount of Aβ peptide in a tissue sample from said rodent;

wherein a decrease in the amount of Aβ peptide in said tissue sample is indicative of a compound that has the ability to decrease *in vivo* levels of said Aβ peptide.

93. (New claim) The method of claim 89 wherein said tissue sample is brain tissue, non-brain tissue, or a body fluid.

94. (New claim) The method of claim 90 wherein said tissue sample is brain tissue, non-brain tissue, or a body fluid.

95. (New claim) The method of claim 91 wherein said tissue sample is brain tissue, non-brain tissue, or a body fluid.

96. (New claim) The method of claim 92 wherein said tissue sample is brain tissue, non-brain tissue, or a body fluid.

97. (New claim) The rodent of claim 39 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I,

M146L (A⇒T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A⇒C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W, S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a Δ exon 9 splice acceptor site deletion mutation (G⇒T with S290C), a Δ exon 9 splice acceptor site deletion mutation (G⇒A with S290C), a Δ exon 9 Finn 4,555 basepair deletion, a Δ intron 4 splice donor consensus sequence G deletion, a C⇒T mutation at position -48 in the 5' promoter, a C⇒G mutation at position -280 in the 5' promoter, or a A⇒G mutation at position -2818 in the 5' promoter.

98. (New claim) The rodent of claim 40 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I, M146L (A⇒T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A⇒C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W, S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a Δ exon 9 splice acceptor site deletion mutation (G⇒T with S290C), a Δ exon 9 splice acceptor site deletion mutation (G⇒A with S290C), a Δ exon 9 Finn 4,555 basepair deletion, a Δ intron 4 splice donor consensus sequence G deletion, a C⇒T mutation at position -48 in the 5' promoter, a C⇒G mutation at position -280 in the 5' promoter, or a A⇒G mutation at position -2818 in the 5' promoter.

REMARKS

Claims 39-64 are pending in the present application. Claims 1-38 and 65-76 have been canceled without prejudice to their presentation in another application as being drawn to non-elected inventions. Claims 43 and 45 have been cancelled. Claims 39-42, 44, 46-52 and 57-60 have been amended, support for which can be found throughout the specification. New claims 77-98 have been added, support for which can be found throughout the specification and, in particular, at, for